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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/234,532	01/21/99	SAPSE A	1398-002

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EXAMINER	
OWENS JR, H	
ART UNIT	**PAPER NUMBER**
1623	4

DATE MAILED: 09/02/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/234,532	Applicant(s) Sapse
	Examiner Howard Owens	Group Art Unit 1623

☐ Responsive to communication(s) filed on _____ .

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-20* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-20* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____ .

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

Specification

Minor informalities

The disclosure is objected to because of the following informalities:

p.2, line 21, a comma appears to be missing after the term "HMB".

P. 11, line 22, absence of a period between "nucleocapsid inhibitors) and "While...".

P. 19, line 21, appears to contain the misspelled word "suspention".

P.22, table, appears to contain the misspelled word "ritonauir".

Appropriate correction is required for this and any other grammatical errors not noted in this office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant specification invites the skilled artisan to experiment. The factors which must be considered in determining undue experimentation are set forth in In re Wands 8USPQ 2d 1400. The factors include:

1) quantity of experimentation necessary,
2) the amount of guidance presented,
3) the presence or absence of working examples,
4) the nature of the invention,
5) the state of the prior art,
6) the predictability of the art,
7) breath of the claims and the
8) level of skill in the art.

Quantity of experimentation necessary, Amount of guidance presented, Presence or absence of working examples

The instant claims of 1-5 and 17 are drawn to a composition for enteral administration comprising at least one anti-HIV drug and at least one cortisol blocker.

As applicant is claiming a composition, there should be provided in the specification sufficient data showing how the claimed invention is made. However, applicant does not provide sufficient data wherein at least one cortisol blocker and at least one anti-HIV drug are used together in a composition. Applicant provides working examples wherein a cortisol blocker is administered subsequent to the administration of an anti-HIV drug, however this does not constitute a composition. The table presented on p. 22 of the specification provides for mixtures of

cortisol blockers separate from mixtures of anti-HIV drugs, but does not provide for a mixture or composition of an anti-HIV drug and a cortisol blocker.

The instant claims of 6-16 and 18-20 are drawn to a method of treating the side effects associated with human immunodeficiency virus in a human comprising administration of at least one anti-HIV drug and at least one cortisol blocker.

In the instant specification applicant provides data from an endurance test performed on rats and a toxicity assay as guidance for the effectiveness of the cortisol/anti-HIV composition; as well as, a dosage table for Procaine, Zn, Ascorbic acid, AZT, ritonavir, 3TC and Epivir to support the instant claims.

Applicant states that the side effects of bone marrow suppression, nausea, myolgia, insomnia, Cushing's syndrome, anemia, disruption of fat metabolism, elevated triglycerides, elevated cholesterol, insulin tolerance, buffalo humps, protease paunches are greatly reduced in Groups 16-24.

However, there is no explanation set forth in the specification that enables a correlation of the data presented in the table to the alleviation or reduction of the targeted side effects. Applicant's statement of a reduction of the side effects does not serve as sufficient evidence or guidance. Moreover, applicant attempts to correlate murine exhaustion points in an endurance test to the alleviation of side effects such as nausea, myolgia, insomnia, Cushing's syndrome, anemia, disruption of fat metabolism, elevated triglycerides, elevated cholesterol, insulin tolerance, buffalo humps, protease paunches does not seem to be a reasonable correlation. Applicant does not provide sufficient data demonstrating actual measurements of each side effect and a corresponding reduction or alleviation.

An Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements, while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved.

In the case of the instant example, the data presented does not sufficiently provide for a reasonable correlation of enablement for the management of the targeted side effects. Moreover, sufficient data is not presented for cortisol blockers with varying structures and effects in the body such as phosphatidylserine, HMB, DHEA, ketaconazole, etc. that would enable one of skill in the art to use these compounds for the management of side effects associated with the treatment of human immunodeficiency virus. In the absence of such data, one of skill in the art would be subject to undue experimentation in the practice of the claimed invention for the management of side effects associated with anti-HIV drug therapy.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2, 3, 7 and 11 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The drugs "BBH-10652, FTC-TBD, NKC-482/TBD, PMPA/Dis-POCPMPA" in claims 2, 3, 7 and 11 are vague and indefinite as these terms have not been established in the art and should be set forth initially as the full written terms or structures which they represent.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted elements are: Claim 6 is indefinite in that applicant has set forth a method for the management of side effects associated with the administration of anti-HIV drug therapy, however applicant has not set forth the drug therapy or associated side effect. Given the number of anti-HIV drug therapies, applicant should set forth in full clear and concise terms what therapies are targeted for treatment as well as the side effects associated therein. Accordingly, dependent claim 9 is rejected as it fails to obviate the rejections set forth in the parent claim(s).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, and 4 are rejected under 35 U.S.C. § 102(b) as being anticipated by each of Knupp et al., Journal of Clinical Pharmacology, vol. (33), 1993; Lemay et al., Int. Conf. AIDS, vol.5,1989; Cloyd et al., Virology, vol. 173, 1990; Harakeh et al., WO 9203052 A, 1992.

Claim 1 is drawn to a composition comprising at least one anti-HIV drug and at least one cortisol blocker.

Claims 2 and 4 are drawn to the composition of claim 1 wherein the anti HIV drug is selected from the group consisting of AZT, DDC, DDI, D4T, 3TC, saquinavir, ritonavir, indinavir, nelfinavir, nevirapine, delevirdine, abacarvir, efavirenz, adefavir, BBH-10652, FTC-TBD, NKC-482/TBD, PMPA/Dis-POCPMPA; and the cortisol blocker is selected from the group consisting of procaine HCl, ascorbic acid, zinc, zinc salts, zinc heptahydrate, lidocaine HCl, phosphatidylserine, HMB, DHEA, ketaconazole, pregnenalone, phenytoin, clonidine and Ipriflavone.

Knupp et al. anticipate the claims cited supra as it teaches the cortisol blocker ketaconazole in combination with the anti HIV drug didanosine(DDI) (see abstract).

Lemay et al. anticipate the claims cited supra as it teaches the cortisol blocker ketaconazole in combination with the anti-HIV drug Zidovudine (AZT) (see abstract).

Cloyd et al. anticipate the claims cited supra as it teaches the cortisol blocker phenytoin (PHT)in combination with the anti-HIV drug AZT (see abstract).

Harakeh et al. anticipate the claims cited supra as it teaches the cortisol blocker ascorbic acid in combination with the anti-HIV drug AZT to inhibit HIV replication and the treatment of AIDS (see abstract).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claim 3, 6-20 are rejected under 35 U.S.C. § 103 as being unpatentable over Devita et al., AIDS,4th edition, pp. 501-504, in combination with Beale, U.S. Patent No. 5,756,469 and Lemay et al., Int. Conf. AIDS, vol.5,1989.

Claim 3 is drawn to a composition comprising at least two anti-HIV drugs and a cortisol blocker.

Claim 6-20 are drawn to a method for the management of side effects associated with the administration of anti-HIV drug therapy comprising administration to a patient a therapeutically effective amount of at least one cortisol blocker.

Beale teaches the use of anti-cortisol compounds such as HMB, DHEA, Ipriflavone and phosphatidylserine in the treatment of patients with AIDS to reduce the catabolic effects associated with AIDS (col.2-col.8, line 19). Beale does not explicitly teach the use of anti-cortisol compounds in a composition with anti-HIV drugs.

Lemay et al. teach the cortisol blocker ketaconazole in combination with the anti- HIV drug Zidovudine (AZT).

Devita et al. teach that combinations of anti-HIV drugs are beneficial in treating HIV infection for several reasons: Two or more drugs may have additive or synergistic interactions that produce better efficacy than with either drug alone, lower doses than those employed in monotherapies- possibly decreasing toxicity, delaying the emergence of a resistant virus that can escape drug inhibition, and targeting of different cellular and tissue reservoirs of the virus; particularly AZT in combination with ddC, ddI or 3TC as the combination of AZT with these agents present stronger synergy over monotherapies or treatment of AZT resistant isolates (DeVita et al., AIDS, 4th edition, pp. 502-504).

A *prima facie* case of obviousness is supported when the prior art alone would have appeared to suggest doing, at the time the invention was made, what the applicant has done. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made that a cortisol blocker could be used in a composition with an anti-HIV drug given that the prior art suggests the use of anti-cortisol compounds in compositions to treat the catabolic effects of AIDS.

One of skill in the art would have been provided with a clear motivation and a reasonable expectation of success to combine the teachings of Beale with that of Lemay and Devita given that any method of treatment would seek to reduce the catabolic effects associated therein, as Lemay and Devita teach the benefits of combination therapies wherein cortisol blockers are used in the treatment of HIV to increase the synergistic effects of an anti-HIV drug and cortisol blockers are shown by Beale to reduce the catabolic effects of the disease itself, whether the catabolic effects are associated with the use of the anti-HIV drug or the disease itself, one of skill would include cortisol blockers in the treatment regime to reduce or alleviate these catabolic effects as an adjunct to a combination therapy.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Howard Owens whose telephone number is (703) 306-4538 . The examiner can normally be reached on Mon.-Fri. from 8:30 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Primary Examiner signing this action, James O. Wilson can be reached on (703) 308-4624 . The fax phone number for this Group is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-1235.

JAMES O. WILSON
PRIMARY EXAMINER
GROUP 1600